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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/357,675	07/20/1999	CARLO M. CROCE	CRO01.NP001	9577

7590 01/13/2003

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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	25

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/357,675	Croce, C.M.
Examiner	**Art Unit**
Scott D. Priebe, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 5, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-24* is/are pending in the application.

4a) Of the above, claim(s) *21-24* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment filed 11/5/02 has been entered. Claims 1-3 and 10-12 have been cancelled. Claims 17-24 have been added.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

Newly submitted claim 17 (in part directed to fragments of 10 nucleotides) and claims 21-24 (entirely) are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons. The originally presented and elected invention was directed to Nit1 genes or nucleic acid encoding a Nit1 protein. Claim 17, in part, is directed to a fragment of at least 10 nucleotides of a DNA encoding a human Nit1 protein and claims 21-24 are directed to fragments of at least 10 nucleotides that are complementary to SEQ ID NO: 1, which encodes NitD. These fragments are not Nit1 genes, nor do they encode Nit1 protein.

The originally presented and elected invention and the newly presented invention are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because a sequence which

encodes SEQ ID NO: 21 (human NIT1) need not contain any particular 10 nucleotides of SEQ ID NO: 1, or need not contain any at all since every wobble base of every codon could be changed and still encode the NIT1 protein. The subcombination has separate utility such as a probe for detecting Nit1 clones or primers for amplification of Nit1 coding sequences. The search of the originally presented and elected invention did not require a search for DNA that comprised only ten nucleotides in common with SEQ ID NO: 1, or with a DNA encoding SEQ ID NO: 21.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 17 (in part, as directed to fragments) and claims 21-24 (entirely) are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Specification

The amendment filed 11/5/02 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the new description of Fig. 6, at page 6, lines 4-5 of the original specification. The original description of Fig. 6 recites: "Highly conserved sequence of human, murine, *D. melanogaster*, and *C. elegans NIT1* genes. (SEQ ID NO: 1).". The first sentence does not apply at all to the contents of Figure 6, which is a nucleotides sequence and predicted amino

acid sequence labeled "NITD", and would be an appropriate description of Fig. 1 which shows an amino acid comparison. No Sequence Listing was filed with the original application. A later filed Sequence Listing was provided indicating that the sequence was human DNA, and by comparison to original Fig. 1 appears to be a human sequence owing to the sequence identity with the human NIT1 amino acid sequence. However no information supporting this label of Fig. 6 being derived from human sequence was presented (see following objection). Comparison to the other sequences of Fig. 1 clearly shows that the NITD sequence of Fig. 6 is not a murine, *D. melanogaster*, or *C. elegans* sequence, as alleged by Applicant on page 5 of the response. The new description of Fig. 6 adds the information that the sequence is a splice variant of some kind. In the response, Applicant provides a description of the difference between the sequence of Fig. 6 and that of SEQ ID NO: 21 (human NIT1 sequence of Fig. 1). Nowhere does Applicant indicate where the original specification discloses that the sequence of Fig. 6 is a splice variant of anything; nor does Applicant provide a declaration attesting to the veracity of the statements made. Original Fig. 6 identifies the sequences as being of NITD, not of NIT1. The specification does not otherwise discuss what Figure 6 is supposed to represent, but goes so far as to distinguish it from nucleic acids encoding a NIT1 protein (compare page 4, lines 14-16 with lines 4-13). Based upon the original disclosure, an appropriate description for Fig. 6 would be --NITD nucleotide (SEQ ID NO: 1) and amino acid sequence (SEQ ID NO: 25).--

Applicant is required to cancel the new matter in the reply to this Office Action.

The amendment filed 3/4/02 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Item <213> of SEQ ID NOs: 1 and 25 identifies these sequences as being human in origin. However, the specification as originally filed does not support this label. Applicant has not indicated where the original specification supports this label, nor has Applicant provided any evidence, e.g. a declaration under 37 CFR 1.132, supporting this label or explaining why it was originally omitted. Applicant is reminded that a Sequence Listing may not contain new matter. 37 CFR 1.821(g).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 101 & 112

Claims 18-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to DNA encoding a human NIT1 protein. The *only* disclosed uses of the claimed invention are for treating or preventing an unspecified disease or disorder in a subject or for diagnosing or screening for the presence of or a predisposition for developing an unspecified disease or disorder in a subject comprising detecting one or more mutations in *NIT1* DNA, RNA or Nit1 protein derived from the subject, which presumably would be human.

The specification does not contain any guidance whatsoever as to how the claimed invention should be used either to treat or to diagnose any disease, nor does it even disclose what disease(s) could be treated or diagnosed. There are no working examples of using the claimed invention for either treatment or diagnosis. There is no evidence presented in the specification that a change in NIT1 function or expression is related to any disease. Consequently, it is completely unpredictable what disease(s), if any, the invention could be used to treat or diagnose.

The specification, on page 7, teaches only *in vitro* multiple tissue northern blots of *NIT1* cDNA probes. However, no further results are reported on the effectiveness of Nit1 protein function having any implication toward the treatment of any particular diseases or disorders. With regard to a method of diagnosing or screening for the presence of or a predisposition for developing a disease or disorder in a subject comprising detecting one or more mutations in *NIT1* DNA or RNA derived from the subject in which the presence of said one or more mutations indicates the presence of the disease or disorder or a predisposition for developing the disease or disorder, the specification fails to teach or suggest any methodology or procedure for a method of diagnosing or screening of any mutations in *NIT1* DNA or RNA correlating to any disease or disorder in any subject as embraced by the claim. The specification only discloses that the pattern of *Nit1* expression was the same in different human cells types, and differed between some mouse cell types, and in mice, was almost identical to the pattern of the expression of Fhit. The specification suggests that the expression pattern in mice support the hypothesis that the NIT1 proteins may act in concert or participate in the same pathway as FHIT (page 14, lines 1-4),

but does not teach what that pathway is. More important, the specification fails to discuss any methods of screening or diagnosing of any disease or disorder in any subject comprising detecting any mutations in *NIT1* DNA or RNA in which the presence of any said mutations would indicate the presence of any disease or disorder. The specification further fails to indicate that any mutations in *NIT1* DNA or RNA would even correlate to any disease or disorder. Thus, it would be unpredictable for one of skill in the art to identify mutations of *NIT1* DNA or RNA which would result in any disease or disorder as embraced by the claimed invention.

There is no evidence of record for any well established use of the claimed invention. The specification does not disclose either a biochemical or biological function for a NIT1 gene or protein. Unknown hypothetical relationships to FHIT function do not suggest any way to use the claimed NIT1 nucleic acids. While the specification teaches that the mammalian NIT1 genes are homologous to plant and bacterial nitrilase genes, it does not teach or suggest that the mammalian NIT1 proteins are nitrilases, or if they were, what nitriles they act on. Applicant has stated on the record (amendment filed 3/27/01) that the NIT1 of the claimed invention "are distinct from the nitrilases", which indicates that the mammalian NIT1 is not a nitrilase. The invention could conceivably be used to determine the biological or biochemical function or activity of NIT1 genes or proteins, and to determine what, if any, relationship the mammalian NIT1 proteins have with FHIT. However, such use amounts to using the invention to further study or characterize itself. Such use does not meet the requirements of §101 or §112, first para. In *Brenner v. Manson*, 148 USPQ 689, 696 (US SupCt., 1966), the Supreme Court noted that

"Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Claims 18-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments filed 11/5/02 have been fully considered to the extent they pertain to this rejection, but they are not persuasive. This new rejection was necessitated by the amendment limiting the claims to DNA encoding *human* NIT1. The cancelled claims embraced prior art sequences of known utility, and thus a rejection for lack of utility of the genus claims was inappropriate. The claims are now limited to previously claimed embodiments that lacked utility at the time the application was filed. Applicant argues that the grounds of rejection apply to methods not the products being claimed. However, Applicant is respectfully requested to re-read the excerpt form MPEP 2164 cited in the response, which states that §112, first para. requires that "the specification describe how to make **and how to use** the invention" (emphasis added). It is the requirement of "how to use" the invention at issue here. The requirements of 35 USC 101 further restrict the type of use to one that is specific, substantial and credible. The

instant invention fails to meet the utility and how to use requirements of §101 and §112, respectively.

Claims 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 19 and 20 depend form claim 17, which is directed to a DNA sequence which encodes a human NIT1 protein. However, the original filed specification did not disclose that SEQ ID NO: 1 was derived from "human" DNA nor did it describe it as encoding a NIT1 protein. Indeed, original Fig. 6 identified it as "NITD". Applicant has provided no evidence that the sequences in Fig. 6 are either human or NIT1. See also objection to the specification above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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